REMARKS/ARGUMENTS

Petition is hereby made under the provisions of 37 CFR 1.136(a) for an extension of three months of the period for response to the Office Action. Our cheque in respect of the prescribed fee is enclosed.

The Examiner considered that the Voluntary Amendment, presumably that submitted June 11, 1999, failed to place the application into sequence compliance.

In particular, the Examiner indicated that the Sequence pages contain new matter, in that the contents disclosed therein do not match those presented in the original specification. The Examiner indicated that SEQ ID No:9 as contained in the Sequence Listing contains 65 amino acids whereas the sequence identified in Table 2, page 17 as being SEQ ID No:9, contains 67 amino acids.

Submitted herewith is a substitute Sequence Listing in hard copy and computer-readable forms. It is hereby stated that the Sequence Listing in hard copy and computer-readable forms are the same and involve no new matter. This Amendment includes direction to substitute the hard copy of the Sequence Listing for the existing one.

Upon examination of the Sequence Listing, it was found that two amino acids had been inadvertently omitted between amino acids 47 and 48 in the Sequence Listing. This matter has been corrected on the enclosed substitute Sequence Listing.

It is submitted that the application is now sequence compliant.

The Examiner required submission of new corrected drawings because the current drawings contain text which is not clearly written, pointing to Figure 2.

The Examiner objected to the drawings on the basis that the data that is presented in the drawings are incomprehensible on the basis that the graphs presented in the drawings lack notation of both X and/or Y-axes, pointing to Figure 1. It is submitted that the Examiner is incorrect and both axes are labelled in Figure 1: X axis: "Count", Y axis: "PMT2LOG".

Nevertheless, a new print of drawings is enclosed which more clearly illustrates the invention depicted in Figures 1, 2 and 3. These amended drawings do not introduce new matter.

The Examiner objected to the specification because of informalities.

In particular, the Examiner noted that page 7, lines 19 to 22 disclose a set of sequences that are capable of binding to HLA-A2 molecules, but the set of sequences is not the same as those disclosed in lines 12 to 14 on page 5 of the specification.

In this regard, the identification of the SEQ ID for CLP-182 has been corrected to SEQ ID NO:7 to be consistent with the remainder of the specification. It is submitted that the informality with respect to the specification has been attended to by this change.

The Examiner objected to claims 1 and 10 because of informalities.

Claims 1 and 10 have been amended to recite in the last line of each claim the provision of a HIV-specific cytotoxic T-cell (CTL) response. The Examiner also mentions claims 2 to 9 and 11. A review of these claims does not reveal the necessity for revision.

It is submitted that the informalities with respect to the claims have been attended to.

The Examiner rejected claims 12 to 15 under 35 USC 101 because the claimed invention is directed to non-statutory subject matter.

This is now the fifth Office Action on this case and this is the first time it has been suggested that these claims, directed to peptides, are directed to non-statutory subject matter. In fact the latest status of these claims, prior to this Office Action, was that claim 12 was allowed and claims 13 to 15 objected to (see Advisory Action dated April 3, 2002). There was never any suggestion that the claims were directed to non-statutory subject matter.

The reason given was that the claims was written used on a product of nature. The Examiner has failed to identify the peptides falling within the scope of claims 12 to 15 which the Examiner regards as products of nature.

Rather than prolong examination on this point, claims 12 to 15 have been amended to recite an isolated peptide.

It is submitted that claims 12 to 15 can no longer be open to objection under 35 USC 101 and hence the rejection should be withdrawn.

The Examiner rejected claim 1 and 4 to 15 under 35 USC 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

In particular, the Examiner indicated that it was unclear what the metes and bounds of the peptide that is recited in claims 12 to 15.

As already noted, claim 15 was previously allowed. There was an objection under 35 USC 112, second paragraph, to claims 13 to 15, but this should have been removed by rewriting claim 13 into an independent form (see Amendment submitted January 17, 2003).

The Examiner noted that claim 12 recites a peptide consisting of amino acids 52 to 116 (SEQ ID NO:9). Thus, the peptide is defined. For further characterization, it is stated that this peptide of defined SEQ ID contains three specific T-cell epitopes that are within three specific parts of the sequence, identified by SEQ ID NOS: 3, 5 and 8.

The language is perfectly clear. It is not seen how the language used could be interpreted as concerning mixtures of peptides, as suggested by the Examiner. For simplicity, claims 12 and 13 have been modified to delete the "containing" part of the claim.

The Examiner also commented on claims 1 and 4 to 11 with respect to limitation "a T-cell inducing HIV molecule" as being vague and indefinite.

The language originally used was "a T-cell inducing HIV-derived molecule". This phrase was objected to in the Office Action of December 8, 1998 and amended in response to the Office Action to the current language, having regard to the Examiner's suggestion. The rejection was not repeated.

The language used is self-explanatory, particularly having regard to the disclosure and the specific exemplification.

The Examiner indicated that the language "and which is a lipopeptide" in claim 10 is unclear. Claim 10 has been amended to remove the phrase "which is a lipopeptide" and to clarify the CLP-175 or CLP-176 is the T-cell inducing HIV molecule.

The Examiner considered there to be insufficient antecedence in claims 9 and 14 for the term "the lipid".

Claims 8 and 13 specify that the peptide is a lipopeptide. A lipopeptide is a peptide which has been lipidated with a lipid. The term "lipopeptide", therefore, provides the antecedent basis for "the lipid" in claims 9 and 14.

Having regard to the revisions to the claims and the comments above, it is submitted that claims 1 and 4 to 15 can no longer be considered to be indefinite and hence the rejection thereof under 35 USC 112, second paragraph, should be withdrawn.

The Examiner rejected claims 1 and 4 to 11 under 35 USC 112, first paragraph, as failing to comply with the written description requirement. In particular, the Examiner considered that the claims contain subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor, at the time the application was filed, had possession of the claimed invention.

The Examiner characterized the rejection as a new matter rejection alleging that support cannot be found in the specification for the recitation "a host possessing MHC class I HLA A2 molecules".

It is not seen how the Examiner can consider that the claims include new matter. On four occasions, the Examiner has stated:

> "Applicants data is only directed to methods using MHC class I HLA A2 molecules"

In this regard, see page 6 of Office Action of December 8, 1998, page 4 of the Office Action of August 20, 1999, page 5 of the Office Action of April 10, 2001 and page 3 of the Office Action of December 19, 2001. In addition reference is made, for example, to Figure 1.

Accordingly, it is submitted that there is no new matter and the rejection of claims 1 and 4 to 11 under 35 USC 112, fist paragraph, on this ground, should be withdrawn.

The Examiner rejected claims 1, 5 to 9 and 11 under 35 USC 112, first paragraph, as failing to comply with the written description requirement. In particular,

the Examiner considered that the claims contain subject matter which was not described in the specification in such a way as to reasonably convey to a person skilled in the art that the inventor, at the time the application was filed, had possession of the claimed invention.

The Examiner indicated that the claims are directed to a genus of T-helper cells while the specification allegedly teaches only SEQ ID NO:10 as the helper molecule.

Applicants invention lies not so much in the use of specific molecules but rather in the protocol for generating an HIV-specific T-cell response in a host. As recited in claim 1, there is first administered to the host a T-helper molecule to prime T-helper cells of the immune system of the host. Thereafter, there is administered to the host a mixture of the T-helper molecule and T-cell inducing HIV molecule to generate the HIV-specific CTL response in the host. The applicants have exemplified this procedure in hosts possessing MHC class I HLA A2 molecules using the specific combinations of materials recited in claim 10.

A person skilled in the art, reading the specification and reviewing applicants data, would readily recognize that molecules other than SEQ ID NO:10 could be used in the protocol described to generate an HIV-specific cytotoxic T-cell response in the host.

It is submitted that the specification provides an adequate written description to support the claims and hence the rejection of claims 1, 5 to 9 and 11 under 35 USC 112, first paragraph, on this ground, should be withdrawn.

The Examiner rejected claims 1, 4 to 9 and 11 under 35 USC 112, first paragraph, as failing to comply with the written description requirement.

In this regard, the Examiner indicated that the T-cell inducing molecules are capable of binding to MHC class I HLA A2 molecules does not necessarily mean that the molecules bind to the HLA A2 molecules.

While not necessarily agreeing with the Examiner, claim 1 has been amended to recite that the T-c ell inducing molecules bind to the MHC class I HLA A2 molecules. Having regard thereto, it is submitted that the written description requirement has been met with respect thereto and hence the rejection of claims 1 and 4 to 11 under 35 USC 112, first paragraph, on this ground, should be withdrawn.

The Examiner rejected claims 1 and 4 to 11 under 35 USC 112, first paragraph, as failing to comply with the enablement requirement. In particular, the Examiner considered that the claims contains subject matter which was not described in the specification in such a way as to enable one skilled in the art to what it pertains, or with which it is most merely connected, to make and/or use the invention.

The Examiner continues to characterize applicants claims as being directed to the treatment, prevention or suppression of the progression of HIV infection in human and non-human animals. That is not what the claims say nor is it what the data presented demonstrates. The claims are directed to the presence of a HIV-specific CTL response in a host.

As mentioned above, the present invention is based on the findings that (1) two nanomer peptides, designated CLP-177 and CLP-72, a hexamer designated CLP-178 and a 12-mer designated CLP-182 of the HIV-1(LAI) REV protein were individually able to bind and stabilize membrane-bound the HLA class 1 molecule, HLA-A2; and (2) that a long peptide (SEQ ID No: 9), encompassing the amino acid residues 52 to 116 of the HIV-1(LAI) Rev protein, and constructed by having a single cholesterol or palmitoyl moiety attached to its amino-(N-) terminus via a KSS linker to form lipopeptides, CLP-176 and CLP-175 respectively, is also capable of eliciting CTL as well as antibody responses in HLA-A2 transgenic mice.

Having regard to their experimental results, applicants have provided a sound immunization protocol for inducing a HIV-specific cytotoxic T-cell response in a host by initial administration of a T-helper molecule to prime the immune system of the host followed by administration of a mixture of the T-helper molecule and a T-cell epitope-containing peptide corresponding to a portion of an HIV antigen.

The invention is illustrated by using, as the T-helper molecule, peptides which correspond to a portion of the hepatitis B virus nucleocapsid antigen and, as the HIV T-cell epitope containing peptide, certain lipopeptides derived from the REV protein, as discussed above. Clearly, however, the invention is applicable to other T-helper cells and other HIV T-cell epitopes containing peptides, and this is reflected in the language adapted.

In general, as recited in claim 1, applicants invention is directed to a method of generating HIV-specific cytotoxic T-cell response in a host. The procedure is a two-step operation, involving an initial administration of a T-helper molecule to provide T-helper cells of the immune system of the host and subsequently administering to the host a mixture of the T-helper molecule a T-cell inducing HIV molecule to generate an HIV-specific CTL response in the host.

Applicants data show the feasibility of the procedure for producing a HIV-specific CTL response and a person skilled in the art would recognize such to be the case. Applicants repeat that these claims do not claim a treatment for HIV infection.

Accordingly, it is submitted that claims 1 and 4 to 11 are fully enabled by the disclosure and hence the rejection thereof under 35 USC 112, first paragraph, on this ground, should be withdrawn.

The Examiner provisionally rejected claims 1 and 4 to 11 under the judicially-created doctrine of obviousness-type double patenting as being unpatentable over claims 1 and 4 to 11 of copending Application No. 09/647,981.

This rejection is a provisional one, since the conflicting claims have not yet been patented. The matter may, therefore, be deferred to a later time.

It is believed that this application is now in condition for allowance and early and favourable consideration and allowance are respectfully solicited.

Respectfully submitted,

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